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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/856,534	09/04/2001	Marco A. Coccia	P 0280624	9135

909 7590 02/25/2004

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EXAMINER	
GAMBEL, PHILLIP	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 02/25/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/856,534	COCCIA, MARCO A.	
	Examiner	Art Unit	
	Phillip Gambel	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 December 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-26* is/are pending in the application.

4a) Of the above claim(s) *1-22,25 and 26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23 and 24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election with traverse of Group IV (claim 24) and the species of "tumor or cancer" as the species of disease, is acknowledged.

Upon reconsideration of applicant's comments, filed 12/2/03, and the recitation of the instant claims, claims 23-24 are under consideration in the instant application.

Applicant's argues that the claimed methods operate to induced a therapeutic protective immune response in any of a number of different types of diseases in which disease-associated antigens can be identified, including diseases in which the antibodies target antigens on virus-infected cells, pathogenic bacteria and tumor cells.

The examiner acknowledges the general applicability of the claimed methods to enhance responses to a variety of antigens. For search and examination purposes, the elected species of tumor or cancer as the targeted antigen / disease is maintained, given that these species are distinct because the targets address differ structures and in turn address different pathological conditions which differ in etiologies and therapeutic endpoints, as pointed out in the previous Office Action.

Claims 1-22 and 25 -26 have been withdrawn from further consideration by the examiner, 37 C.F.R. § 1.142(b) as being drawn to nonelected inventions and species

2. The application is required to be reviewed and all spelling, TRADEMARKS, and like errors corrected.

Trademarks should be capitalized or accompanied by the ™ or ® symbol wherever they appear and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the trademarks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Appropriate corrections are required

3. The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 23-24 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The specification broadly describes and the claims recite as part of the invention the following:
"the chimeric protein of claim 10" where claim 10 recites:
"A chimeric protein comprising a variable region binding domain from a disease antigen-specific antibody at its amino terminus and an extracellular binding portion of an immunostimulatory ligand at its carboxyl terminus, wherein said immunostimulatory ligand is a CD40 ligand".

Applicant has not provided a sufficient written description of the myriad of "chimeric proteins comprising a variable region binding domain from a disease antigen-specific antibody at its amino terminus".

Given the well known polymorphism of immunoglobulins / antibodies and the absence of a recitation of "disease antigen specificity", there is insufficient written description of "chimeric protein" employed in the claimed methods. The structure of the claimed chimeric proteins would have been expected to vary and the skilled artisan would not have able to predict the structure, given the nature of high polymorphism in immunoglobulin structure. The skilled artisan would not have envisioned the detailed structure of the chimeric proteins, encompassing an antibody in the absence of an antigen specificity. Conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

The skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides (proteins) and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.

One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481, 1483. In Fiddes v. Baird, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Thus, the specification fails to describe the "chimeric proteins, particularly with respect to the antibody element in the absence of an antigen specificity" in the claimed methods. The Court further elaborated that generic statements are not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. Finally, the Court indicated that while applicants are not required to disclose every species encompassed within a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, defined by nucleotide sequence, falling within the scope of the genus, See The Regents of the University of California v. Eli Lilly and Company, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Therefore, there is insufficient written description for the "chimeric proteins, particularly with respect to the antibody element in the absence of an antigen specificity" in the claimed methods under the written description provision of 35 USC 112, first paragraph.

Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.)

Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

5 Claims 23-24 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention

Applicant has not provided sufficient biochemical information, such as the sequence information or as providing the hybridomas of a number of disease antigen-specific antibodies that distinctly identifies disease antigen-specific-specific antibodies in the absence of an antigen specificity that enables the skilled artisan to obtain the antibody element of the chimeric proteins employed in the claimed methods encompassed by the claimed invention.

Given the well known polymorphism of immunoglobulins / antibodies; it would have been undue experimentation to derive the vast repertoire of antibody specificities to the any disease antigen that are incorporated into the claimed chimeric proteins employed in the claimed methods.

Without sufficient guidance and given the well known polymorphism of immunoglobulins / antibodies; it would be unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue to determine the vast repertoire of disease antigen-specific antibodies in the absence of an antigen specificity to construct the claimed chimeric proteins in the claimed methods.

Reasonable correlation must exist between the scope of the claims and scope of enablement set forth.

The specification does not describe nor enable disease antigen-specific antibodies incorporated into the claimed chimeric proteins employed in the claimed methods, commensurate in scope with the claimed invention.

6. Claims 23 -24 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 23-24 are indefinite in that it depends on a non-elected invention.
Applicant should amend the claims to recite claims 24-25 as independent claims.

B) Claim 24 is indefinite in that the therapeutic endpoint of "treating a disease in a patient in need of such treatment" is ill-defined and ambiguous, as no clear endpoint is recited. The ordinary artisan would not be apprised of the metes and bounds of the claims.

C) Applicant should specifically point out the support for any amendments made to the disclosure. See MPEP 714.02 and 2163.06

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office Action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 23-24 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Whitlow et al. (U.S. Patent No. 5,767,260) AND/OR Denney et al. (U.S. Patent No. 5,972,334) in view of Grabstein (U.S. Patent No. 5,747,024) and Armitage et al. (U.S. Patent No. 6,290,972).

Whitlow et al. teach chimeric antigen-binding antibody fusion proteins and pharmaceutical compositions encompassed by the claimed invention, including the linkers, antigen-binding fragments encompassed by the claimed invention, for using the proteins as a carrier to target and to treat medical conditions and pathologies, including tumor specificities (see entire document, including Background of the Invention; Summary of the Invention; Detailed Description of the Invention) . For example, Whitlow et al. teach chimeric antibody constructs which comprise immunoeffector molecules at the carboxyl terminus (e.g. see column 3, paragraph 6; column 13, lines 1-13).

Denney et al. teach antigen-binding antibody fusion proteins and pharmaceutical compositions encompassed by the claimed invention, including the linkers, antigen-binding fragments encompassed by the claimed invention to target and to treat tumors and to deliver vaccines (see entire document, including Background of the Invention; Summary of the Invention; Detailed Description of the Invention). For example, Denney et al. teach immunoglobulin molecules comprising recombinant variable regions derived from a patient's lymphoma cell from a patient's lymphoma cell linked to an immune-enhancing cytokine (e.g. see paragraph 3 of the Summary of the Invention on column 3 and Production of Custom Multivalent Vaccines for the Treatment of Lymphoma and Leukemia on columns 31-33 and Administration of Tumor-specific Ig on columns 62-64).

Whitlow et al. and Denney et al. differ from the claimed invention by not disclosing the use of the immunostimulatory ligand CD40L in such constructs.

Grabstein et al. teach that CD40L is a vaccine adjuvant (column 4, paragraph 1); that adjuvants refers to substances that enhance, augments or potentiates the host's immune response to a vaccine antigen (column 3, paragraph 3); and that tumor antigens are appropriate targets of vaccines (column 3, paragraph 2).

Armitage et al. teach the administration of CD40L to augment vaccine responses (see entire document, particularly, columns 10-11, overlapping paragraph, and Claims).

Given the adjuvant properties of the CD40L at the time the invention was made as taught by Grabstein and Armitage et al.; one of ordinary skill in the art at the time the invention was made would have been motivated to select CD40L as the cytokine or adjuvant in chimeric antibody- cytokine fusion proteins, as taught by Whitlow et al. and Denney et al. to deliver the immunoenhancing properties of the CD40L to stimulate anti-tumor responses. From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

9. No claim is allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (571) 272-0844. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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February 17, 2004